

- b) an isolated nucleic acid molecule which hybridizes under conditions of high stringency to DNA having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds to hTNF $\alpha$ .
3. (Amended) An isolated nucleic acid molecule selected from the group consisting of:
- C<sub>2</sub>
- a) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds to hTNF $\alpha$ , wherein said nucleic acid molecule hybridizes under conditions of moderate stringency to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of [SEQ ID NO: 2 or] SEQ ID NO: 4 [, or] ;
- b) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds to hTNF $\alpha$ , wherein said nucleic acid molecule hybridizes under conditions of moderate stringency to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2; and
- c) a complement of [said] an isolated nucleic acid molecule of a) or b).
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5. (Amended) An isolated nucleic acid molecule selected from the group consisting of:
- C<sub>3</sub>
- a) an isolated nucleic acid molecule which, when expressed with a molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 and a gene encoding an IgG1 immunoglobulin constant region, [encoding] encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 [or SEQ ID NO: 5], or a fragment [or derivative] thereof, [wherein said polypeptide] which binds hTNF $\alpha$  [, or];
- b) an isolated nucleic acid molecule which, when expressed with a molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 5, or a fragment thereof, which binds hTNF $\alpha$ ; and
- c) a complement of [said] the isolated nucleic acid molecule of a) or b).
- C

- C4
7. (Amended) An isolated nucleic acid molecule comprising a sequence selected from the group consisting of:
- a) SEQ ID NO: 2;
  - b) the complementary strand of SEQ ID NO: 2;
  - c) DNA sequences that [specifically] hybridize under conditions of high stringency to the complementary sequence of SEQ ID NO: 2, and which, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encode a polypeptide which binds hTNF $\alpha$ ; and
  - d) RNA sequences transcribed from the sequences of a), b), or c).
8. (Amended) An isolated nucleic acid molecule comprising a sequence selected from the group consisting of:
- a) SEQ ID NO: 4;
  - b) the complementary strand of SEQ ID NO: 4;
  - c) DNA sequences that [specifically] hybridize under conditions of high stringency to the complementary sequence of SEQ ID NO: 4, and which, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encode a polypeptide which binds hTNF $\alpha$ ; and
  - d) RNA sequences transcribed from the sequences of a), b), or c).
- C5
17. (Amended) A method of manufacturing a polypeptide, said polypeptide selected from the group consisting of:
- a) a polypeptide comprising the amino acid sequence [selected from the group consisting] of SEQ ID NO: 3 [and SEQ ID NO: 5] or a fragment [or derivative] thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 5 and an IgG1 constant region, binds to hTNF $\alpha$ ; and
  - b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 or a fragment thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 3 and an IgG1 constant region, binds to hTNF $\alpha$ .
- C

C5 comprising the steps of expressing said polypeptide in a recombinant host cell which comprises a nucleic acid molecule which encodes said polypeptide operably linked to a promoter sequence.

18. An isolated nucleic acid molecule selected from the group consisting of:

- C6
- a) an isolated nucleic acid molecule which hybridizes to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ ;
  - b) an isolated nucleic acid molecule which hybridizes to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ ; and
  - c) a complement of an isolated nucleic acid molecule of a) or b).

19. An isolated nucleic acid molecule selected from the group consisting of:

- a) an isolated nucleic acid molecule which hybridizes to DNA having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ ;
  - b) an isolated nucleic acid molecule which hybridizes to DNA having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS, and incubation with rotation for 15 minutes at 68° C, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ ; and
- C

- c) a complement of an isolated nucleic acid molecule of a) or b).
20. An isolated nucleic acid molecule selected from the group consisting of:
- a) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ , wherein said nucleic acid molecule hybridizes to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4 under wash conditions of wash solution of 42° C 0.2x SSC/0.1% SDS and incubation with rotation for 15 minutes at 42° C;
  - b) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds hTNF $\alpha$ , wherein said nucleic acid molecule hybridizes to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2 under wash conditions of wash solution of 42° C 0.2x SSC/0.1% SDS and incubation with rotation for 15 minutes at 42° C; and
  - c) a complement of an isolated nucleic acid molecule of a) or b).
21. An isolated nucleic acid molecule comprising a DNA sequence that hybridizes to the complementary sequence of SEQ ID NO: 2 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C, said molecule, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encoding a polypeptide which binds hTNF $\alpha$ , or an RNA sequence transcribed from the DNA sequence.
22. An isolated nucleic acid molecule comprising a DNA sequence that hybridizes to the complementary sequence of SEQ ID NO: 4 under wash conditions of wash solution of 68° C 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C, said molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encoding a polypeptide which binds hTNF $\alpha$ , or an RNA sequence transcribed from the DNA sequence.
23. An isolated nucleic acid molecule selected from the group consisting of:
- a) an isolated nucleic acid molecule which hybridizes under conditions of high stringency to a nucleic acid molecule having the complementary sequence of the

nucleotide sequence of SEQ ID NO: 2, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ ;

- b) an isolated nucleic acid molecule which hybridizes under conditions of high stringency to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ ; and
- c) a complement of an isolated nucleic acid molecule of a) or b).

24. An isolated nucleic acid molecule selected from the group consisting of:

- a) an isolated nucleic acid molecule which hybridizes under conditions of high stringency to DNA having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ ; and
- b) an isolated nucleic acid molecule which hybridizes under conditions of high stringency to DNA having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4, wherein said isolated nucleic acid molecule, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ .

25. An isolated nucleic acid molecule selected from the group consisting of:

- a) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ , wherein said nucleic acid molecule hybridizes under conditions of moderate stringency to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 4;
- b) an isolated nucleic acid molecule which, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide which binds and inhibits hTNF $\alpha$ , wherein

said nucleic acid molecule hybridizes under conditions of moderate stringency to a nucleic acid molecule having the complementary sequence of the nucleotide sequence of SEQ ID NO: 2; and

- c) a complement of an isolated nucleic acid molecule of a) or b).

26. An isolated nucleic acid molecule selected from the group consisting of:

- a) an isolated nucleic acid molecule which, when expressed with a molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 3, or a fragment thereof, which binds and inhibits hTNF $\alpha$ ;
- b) an isolated nucleic acid molecule which, when expressed with a molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 and a gene encoding an IgG1 immunoglobulin constant region, encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 5, or a fragment thereof, which binds and inhibits hTNF $\alpha$ ; and
- c) a complement of the isolated nucleic acid molecule of a) or b).

27. An isolated nucleic acid molecule comprising a sequence selected from the group consisting of:

- a) SEQ ID NO: 2;
- b) the complementary strand of SEQ ID NO: 2;
- c) DNA sequences that hybridize under conditions of high stringency to the complementary sequence of SEQ ID NO: 2, and which, when expressed with a molecule having the sequence of SEQ ID NO: 4 and a gene encoding an IgG1 immunoglobulin constant region, encode a polypeptide which binds and inhibits hTNF $\alpha$ ; and
- d) RNA sequences transcribed from the sequences of a), b) or c).

28. An isolated nucleic acid molecule comprising a sequence selected from the group consisting of:

- a) SEQ ID NO: 4;
- b) the complementary strand of SEQ ID NO: 4;
- c) DNA sequences that hybridize under conditions of high stringency to the complementary sequence of SEQ ID NO: 4, and which, when expressed with a molecule having the sequence of SEQ ID NO: 2 and a gene encoding an IgG1

immunoglobulin constant region, encode a polypeptide which binds and inhibits hTNF $\alpha$ ; and

- d) RNA sequences transcribed from the sequences of a), b) or c).

29. A method of manufacturing a polypeptide, said polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or a fragment thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 5 and an IgG1 constant region, binds and inhibits hTNF $\alpha$ ; and

b) a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 or a fragment thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 3 and an IgG1 constant region, binds and inhibits hTNF $\alpha$ ,

comprising the step of expressing said polypeptide in a recombinant host cell which comprises a nucleic acid molecule which encodes said polypeptide operably linked to a promoter sequence.

30. A method of manufacturing a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or a fragment thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 5 and an IgG1 constant region, binds to hTNF $\alpha$ , comprising the step of expressing a nucleic acid molecule which encodes said polypeptide, said nucleic acid molecule operably linked to a promoter sequence, with a nucleic acid molecule encoding a peptide comprising the amino acid sequence of SEQ ID NO: 5.

31. The method of Claim 30 wherein the nucleic acid molecule encoding the polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or a fragment thereof is expressed with a gene encoding an IgG1 immunoglobulin constant region.

32. A method of manufacturing a polypeptide comprising the amino acid sequence of SEQ ID NO: 5 or a fragment thereof wherein said polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 3 and an IgG1 constant region, binds to hTNF $\alpha$ , comprising the step of expressing a nucleic acid molecule which encodes said polypeptide, said nucleic acid molecule operably linked to a promoter sequence, with a

nucleic acid molecule encoding a peptide comprising the amino acid sequence of SEQ ID NO: 3.

33. The method of Claim 32 wherein the nucleic acid molecule encoding the polypeptide comprising the amino acid sequence of SEQ ID NO: 5 or a fragment thereof is expressed with a gene encoding an IgG1 immunoglobulin constant region.
34. A method of manufacturing a polypeptide encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 2 or a fragment thereof wherein said polypeptide, when expressed with a peptide encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 4 and an IgG1 constant region, binds to hTNF $\alpha$ , comprising the step of expressing a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 2 or a fragment thereof, said nucleic acid molecule operably linked to a promoter sequence, with a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 4.
35. The method of Claim 34 wherein the nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 2 or a fragment thereof is expressed with a gene encoding an IgG1 immunoglobulin constant region.
36. A method of manufacturing a polypeptide encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 4 or a fragment thereof wherein said polypeptide, when expressed with a peptide encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 2 and an IgG1 constant region, binds to hTNF $\alpha$ , comprising the step of expressing a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 4 or a fragment thereof, said nucleic acid molecule operably linked to a promoter sequence, with a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 2.
37. The method of Claim 36 wherein the nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 4 or a fragment thereof is expressed with a gene encoding an IgG1 immunoglobulin constant region.
38. The method of Claim 30 wherein the polypeptide, when expressed with a peptide comprising the amino acid sequence of SEQ ID NO: 5 and an IgG1 constant region, binds and inhibits hTNF $\alpha$ .